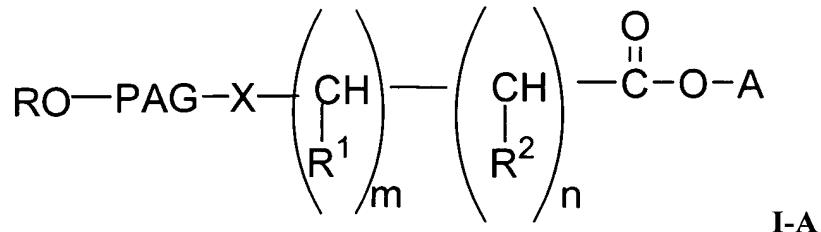


**In the Claims:**

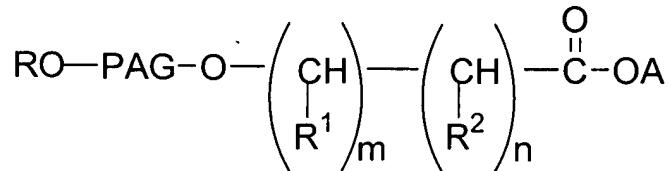
1. (Currently Amended) A compound of the formula



wherein R, R<sub>1</sub> and R<sub>2</sub> are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons; n is an integer of from 0 to 1; m is an integer of from 4 to 8; and A is a hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester

or hydrolyzable esters thereof wherein A is hydrogen, wherein said PAG residue has a molecular weight of about 10,000 to about 40,000 Daltons when X is O.

2. (Original) The compound of claim 1 having the formula

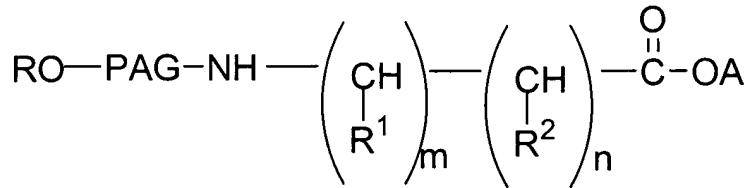


**I-A1**

wherein A, R, PAG, R<sup>1</sup>, R<sup>2</sup>, m and n are as above.

3. (Original) The compound of claim 2 wherein A is hydrogen.
4. (Original) The compound of claim 3 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.
5. (Original) The compound of claim 4 wherein R is methyl.
6. (Original) The compound of claim 5 wherein n is 0 and m is 4.
7. (Original) The compound of claim 5 wherein PEG has a molecular weight of from 10,000 to 40,000.
8. (Original) The compound of claim 6 wherein PEG has a molecular weight of from 20,000 to about 35,000.
9. (Original) The compound of claim 2 wherein A is an activated leaving group.
10. (Original) The compound of claim 9 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.
11. (Original) The compound of claim 9 wherein R is methyl.
12. (Original) The compound of claim 11 wherein n is 0 and m is 4.
13. (Original) The compound of claim 12 wherein PEG has a molecular weight of from 10,000 to 40,000.
14. (Original) The compound of claim 13 wherein PEG has a molecular weight of from 20,000 to about 35,000.

15. (Original) The compound of claim 1 wherein said compound has the formula



I-A2

wherein A, R, PAG, R<sup>1</sup>, R<sup>2</sup>, m and n are as above.

16. (Original) The compound of claim 15 wherein A is hydrogen.

17. (Original) The compound of claim 16 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

18. (Original) The compound of claim 17 wherein R is methyl.

19. (Original) The compound of claim 18 wherein n is 0 and m is 4.

20. (Original) The compound of claim 19 wherein PEG has a molecular weight of from 10,000 to 40,000.

21. (Original) The compound of claim 20 wherein PEG has a molecular weight of from 20,000 to about 35,000.

22. (Original) The compound of claim 18 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

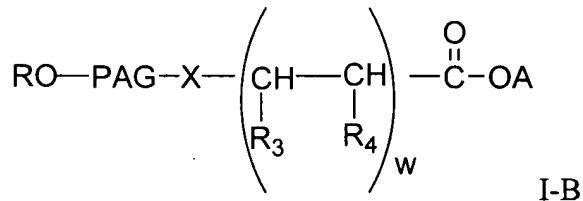
23. (Original) The compound of claim 22 wherein R is methyl.

24. (Original) The compound of claim 23 wherein n is 0 and m is 4.

25. (Original) The compound of claim 24 wherein PEG has a molecular weight of from 10,000 to 40,000.

26. (Original) The compound of claim 25 wherein PEG has a molecular weight of from 20,000 to about 35,000.

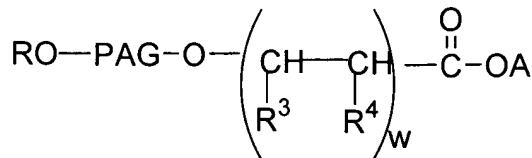
27. (Original) The compound of formula



wherein R is hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons ; w is an integer of from 1 to 3; and one of R<sub>3</sub> and R<sub>4</sub> is lower alkyl and the other is hydrogen or lower alkyl; and A is a hydrogen or an activated leaving group which when taken together with its attached oxygen forms an ester;

or hydrolyzable esters thereof wherein A is hydrogen.

28. (Original) The compound of claim 27 wherein said compound is



I-B1

wherein A, R, PAG,  $\text{R}^3$ ,  $\text{R}^4$ , w and n are as above.

29. (Original) The compound of claim 28 wherein A is hydrogen.

30. (Original) The compound of claim 29 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

31. (Original) The compound of claim 30 wherein R is methyl.

32. (Original) The compound of claim 31 wherein w is 1.

33. (Original) The compound of claim 32 wherein PEG has a molecular weight of from 10,000 to 40,000.

34. (Original) The compound of claim 33 wherein PEG has a molecular weight of from 20,000 to about 35,000.

35. (Original) The compound of claim 28 wherein A is an activated leaving group.

36. (Original) The compound of claim 35 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

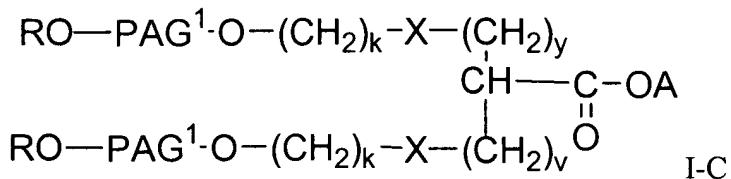
37. (Original) The compound of claim 36 wherein R is methyl.

38. (Original) The compound of claim 37 wherein w is 1.

39. (Original) The compound of claim 38 wherein PEG has a molecular weight of from 10,000 to 40,000.

40. (Original) The compound of claim 39 wherein PEG has a molecular weight of from 20,000 to about 35,000.

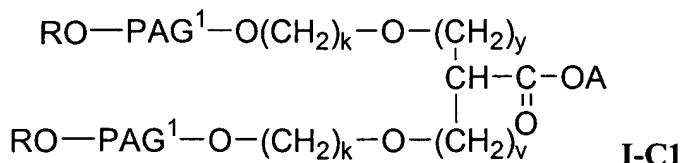
41. (Original) The compound of formula



wherein R is hydrogen or lower alkyl, X is -O- or -NH-, A is a hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester, PAG<sup>1</sup> is a divalent residue of a polyalkylene glycol resulting from the removal of both of the terminal hydroxy groups, said residue having a molecular weight of from about 500 to about 25,000 Daltons, y is an integer from 0 to 3 and v is an integer from 1 to 3; and k is an integer from 1 to 2;

or hydrolyzable esters thereof wherein A is hydrogen.

42. (Original) The compound of claim 41 wherein said compound has the formula



wherein R, PAG<sup>1</sup>, A v, y and k are all as above.

43. (Original) The compound of claim 42 wherein A is hydrogen.

44. (Original) The compound of claim 43 wherein PAG<sup>1</sup> is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

45. (Original) The compound of claim 42 wherein each PAG<sup>1</sup> residue has a molecular weight of 500 to 15,000.

46. (Original) The compound of claim 42 wherein A is a leaving group.

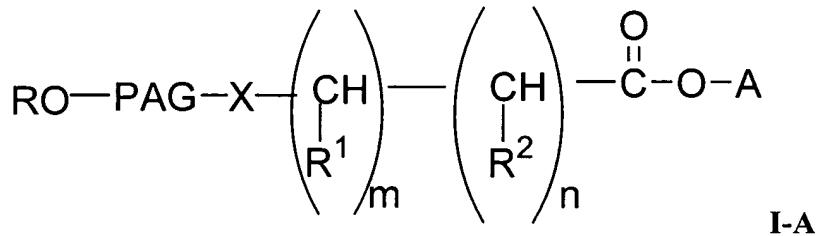
47. (Original) The compound of claim 46 wherein said leaving group is N-hydroxysuccinimidyl.

48. (Original) The compound of claim 47 wherein PAG<sup>1</sup> is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

49. (Original) The compound of claim 48 wherein R is methyl.

50. (Original) The compound of claim 49 wherein each PEG residue has a molecular weight of from 500 to 10,000.

51. (Currently Amended) A process for producing an activated ester of the formula:



wherein R, R<sub>1</sub> and R<sub>2</sub> are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons; n is an integer of from 0 to 1; m is an integer of from 4 to 8; and A is a hydrogen or an activated

leaving group which when taken together with its attached oxygen atom forms an ester

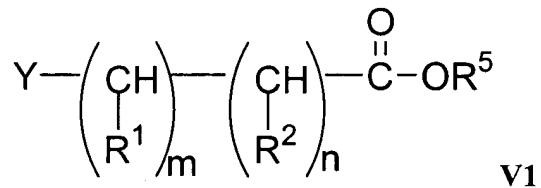
comprising, condensing a compound of the formula:



V

wherein R, and PAG are as above, and V is —OH or —NH<sub>2</sub>,

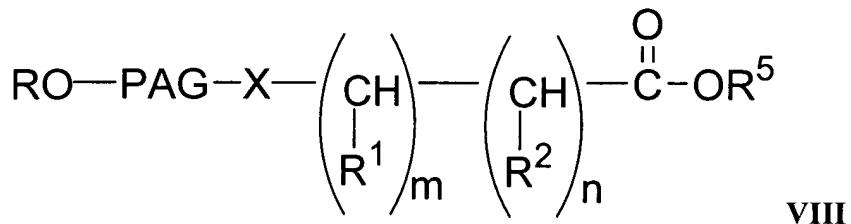
with the compound of the formula:



wherein R<sup>5</sup> forms a hydrolyzable ester protecting group and Y is halide and

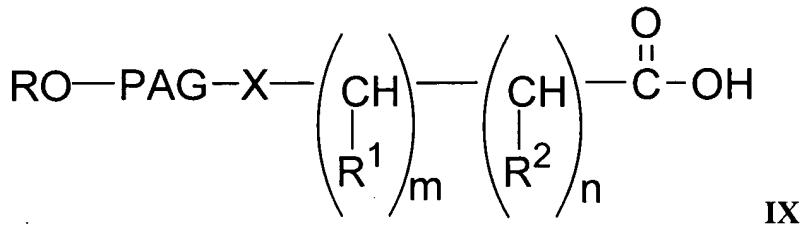
R<sup>1</sup>, R<sup>2</sup>, m, and n, are as above,

to produce an ester of the formula



wherein R, PAG, X, R<sup>1</sup>, R<sup>2</sup>, R<sup>5</sup>, m and n are as above,

hydrolyzing said ester to form a free acid of the formula:



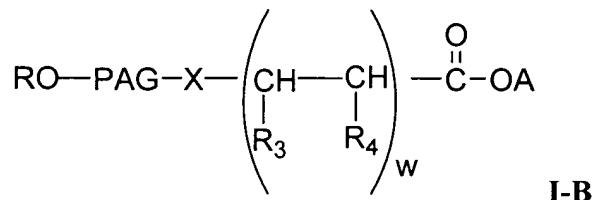
wherein R, PAG, X, R<sup>1</sup>, R<sup>2</sup>, m and n are as above,

and reacting said free acid with a halide of an activated leaving group in the presence of a coupling agent to produce said activated ester,

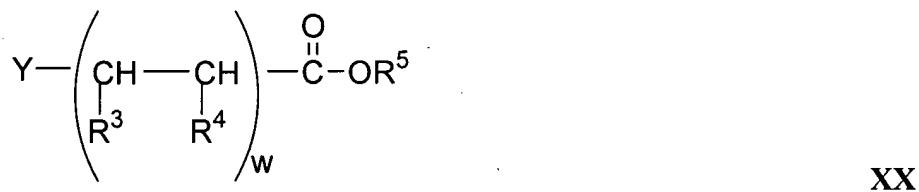
and wherein said PAG residue has a molecular weight of about 10,000 to about 40,000 Daltons when X is O.

52. (Currently Amended) The process of claim 51 wherein said leaving group is a N-hydroxysuccinimidyl group-58.

53. (Original) A process for producing an activated ester of the formula:



wherein R is hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkyleneglycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons; w is an integer of from 1 to 3; and one of R<sub>3</sub> and R<sub>4</sub> is lower alkyl and the other is hydrogen or lower alkyl; and A is a hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester comprising, condensing a compound of the formula:



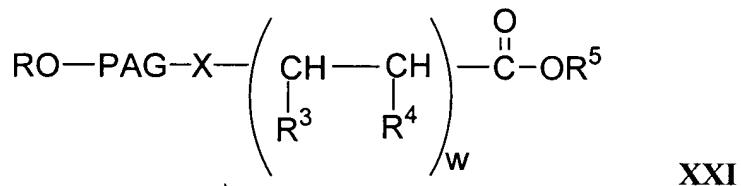
wherein w, Y, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are as above, Y is halide and R<sup>5</sup> forms a hydrolyzable protecting group

with a compound of the formula:

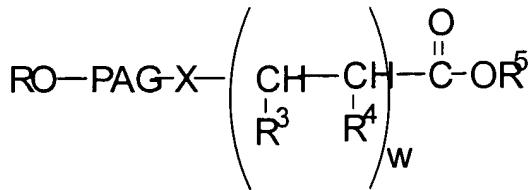


V

wherein R, and PAG are as above, V is -OH or -NH<sub>2</sub>,  
to produce an ester of the formula:



wherein w, R, PAG, X, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are as above  
hydrolyzing said ester to form a free acid of the formula:



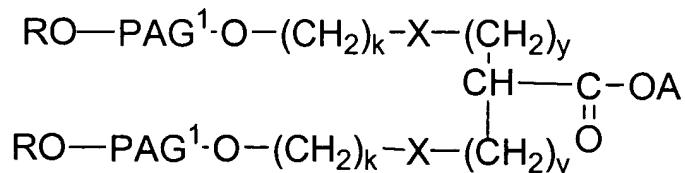
XXII

wherein R, PAG, X, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are as above,

and reacting said free acid with a halide of an activated leaving group in the presence of a coupling agent to produce said activated ester.

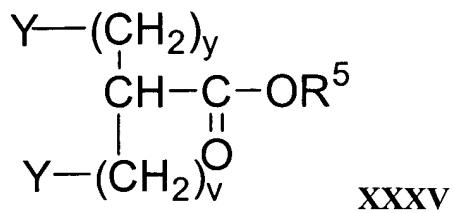
54. (Original) The process of claim 53 wherein said leaving group is a N-hydroxysuccinimidyl group.

55. (Original) A process for producing an activated ester of the formula:



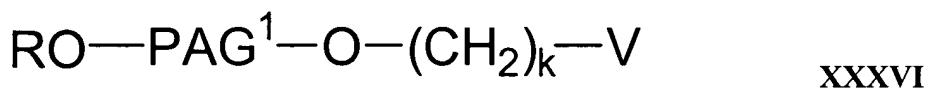
I-C

wherein R is hydrogen or lower alkyl, X is -O- or -NH, A is a hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester, PAG<sup>1</sup> is a divalent residue of a polyalkylene glycol resulting from the removal of both of the terminal hydroxy groups, said residue having a molecular weight of from about 500 to about 25,000 Daltons, y is an integer from 0 to 3 and v is an integer from 1 to 3; and k is an integer from 1 to 2, comprising, condensing a compound of the formula:

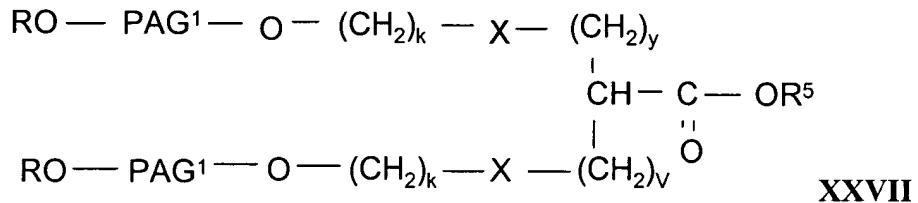


wherein Y is halide, y and v are as above, and R<sup>5</sup> forms a hydrolyzable ester protecting group

with a compound of the formula

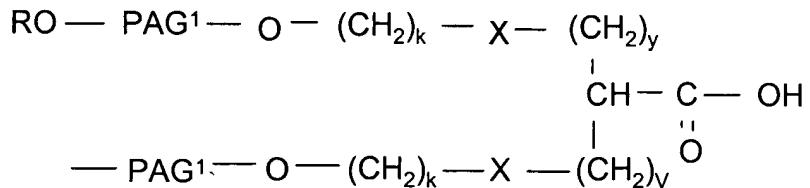


wherein R, PAG<sup>1</sup> and k are as above, V is -OH or -NH<sub>2</sub>,  
to produce an ester of the formula:



wherein R, PAG<sup>1</sup>, X, R<sup>5</sup>, k, v and y are as above,

hydrolyzing said ester to form a free acid of the formula:

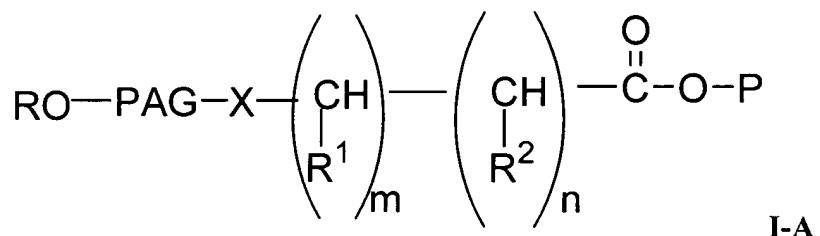


wherein R, PAG<sup>1</sup>, X, k, v and y are as above,

and reacting said free acid with a halide of an activated leaving group in the presence of a coupling agent to produce said activated ester.

56. (Original) The process of claim 55 wherein said leaving group is N-hydroxysuccinimidyl.

57. (Original) A conjugate of the formula



wherein P is a residue of a biopharmaceutical having a terminal hydroxy group wherein the terminal hydroxy group is removed, R, R<sub>1</sub> and R<sub>2</sub> are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons; n is an integer of from 0 to 1; and m is an integer of from 4 to 8.

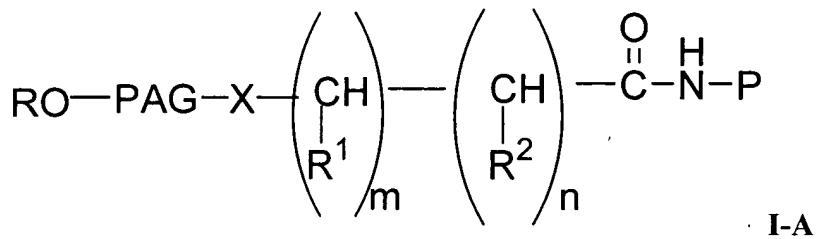
58. (Original) The conjugate of claim 57 wherein P is a glycoside.

59. (Original) The conjugate of claim 58 wherein P is a residue of AZT.

60. (Original) The conjugate of claim 57 wherein X is -O-.

61. (Original) The conjugate of claim 60 wherein PAG is a polyethylene glycol residue having a molecular weight of 10,000 to 15, 000.

62. (Original) A conjugate of the formula



wherein P is a residue of a biopharmaceutical having a terminal hydroxy group wherein the terminal hydroxy group is removed, R, R<sub>1</sub> and R<sub>2</sub> are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons; n is an integer of from 0 to 1; and m is an integer of from 4 to 8.

Filed: 07/22/2003

63. (Original) The conjugate of claim 62 wherein P is a residue of a protein or polypeptide.
64. (Original) The conjugate of claim 63 wherein X is -O-.
65. (Original) The conjugate of claim 64 wherein PAG is a polyethylene glycol residue having a molecular weight of about 10,000 to 15,000.
66. (Original) The conjugate of claim 63 wherein P is the polypeptide T-20 having a sequence according to SEQ ID NO: 1.
67. (Original) The conjugate of claim 64 wherein R is methyl.